REMARKS

A Petition for Extension of Time is being concurrently filed with this Amendment. Thus, this Amendment is being timely filed.

Applicant respectfully requests the Examiner to reconsider the present application in view of the foregoing amendments to the claims and the following remarks.

Status of the Claims

Claims 9, 12, 15, 18 and 21-30 are currently pending in the present application. Claims 9, 12, 15, 18 and 21 have been withdrawn from consideration. The Office Action is Final. Claim 30 is new. Claim 30 is an independent claim which incorporates claims 22-26 and 29. Thus no new matter has been added.

Based upon the above considerations, entry of the present amendment is respectfully requested.

Rejection Under 35* U.S.C. § 103(a), *Obviousness

Claims 22-29 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Konzak *et al.*, U.S. Patent No. 6,362,393(hereinafter "Konzak *et al.*") in view of Forreiter *et al.*, *"Stable Transformation of an Arabidopsis Cell Suspension Culture With Firefly Luciferase Providing a Cellular System for Analysis of Chaperone Activity In Vivo,"* The Plant Cell, *vol. 9, pp. 2171-2181 (1997)* (Hereinafter "Forreiter *et al.*") in light of Pierce Biotechnology, Inc., Technical resource 1/2005, "*Convert between times gravity (x g) and centrifuge rotor speed (RPM)*" (Hereinafter "Pierce").

The Examiner asserts that Konzak *et al.* disclose a method of centrifuging plant tissues of rice or corn at the acceleration of 100G for 3 minutes prior to gene introduction. The Examiner also asserts that Konzak *et al.* teach that gene transformation could occur at any time of the procedure by using *Agrobacterium tumifaciens*. The Examiner also states that Konzak *et al.* do not teach the centrifugation speed of 1000G to 150,000G.

The Examiner also asserts that Forreiter *et al.* disclose a method of gene transfer of *Arabidopsis thaliana,* an Angiosperm, cells by *Agrobacterium* comprising centrifuging the cells for one minute at 600G. Additionally, the Examiner also asserts it would have been obvious to one of ordinary skill in the art to use the method of promoting gene introduction into plant cells by centrifuging the plant cells or plant tissues before gene introduction by applying *Agrobacterium* as taught by Konzak *et al.*, and to modify that method by adjusting the centrifugal acceleration as taught by Forreiter et al given the advantage of separating the tissues at higher speed.

Additionally the Examiner noted that Pierce discloses "centrifugation speed and time often are not critical *factors in* routine sampling-handling...." Applicants respectfully traverse.

A proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See* M.P.E.P. § 2143.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), has provided the controlling framework for an obviousness analysis. A proper analysis under § 103(a) requires consideration of the four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467.

The teaching, suggestion, motivation test is a valid test for obviousness, but one which cannot be too rigidly applied. *See KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385, 1395 (U.S. 2007). While the courts have adopted a more flexible teaching/suggestion/motivation (TSM) test in connection with the obviousness standard based on the *KSR v. Teleflex* case which involved a mechanical device in a relatively predictable technological area, it remains true that, despite this altered standard, the courts recognize inventors face additional barriers in relatively unpredictable technological areas as noted in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007) (since TSM test can provide helpful insight if it is not applied as rigid and mandatory formula, and since, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led chemist to modify known compound, in particular manner, in order to establish *prima facie* obviousness of new compound).

The Examiner mischaracterizes the disclosure of the Konzak *et al.* reference as well as the combination of Konzak *et al.* to that of the other cited references. As the Examiner indicated in the Office Action dated January 10, 2007 (hereinafter "Office Action"), page 3, Konzak *et al.* do not disclose or teach the centrifugation speeds for more efficient transformation. Additionally

the Examiner mischaracterizes the Konzak *et al.* procedure in general as a procedure that the centrifugation step leads a skilled artisan to be able to transform cells more efficiently by such a slow centrifugation speed.

Konzak *et al.* discloses a method in which wheat plants are produced by selecting wheat spikes containing microspores (precursor cells to pollen) by isolating the microspores by centrifugation at 100G. The density gradient centrifugation step, performed at 100G, is for **isolation of the microspores from plant debris and other cell organelles.** This is a basic purification step that is preparative in nature. Additionally a skilled artisan would recognize that for such a preparative procedure to remove debris from a sample, high *g* centrifugation would be unnecessary and highly inefficient for such a preparative purpose.

Konzak *et al.* takes the purified plant preps (*i.e.*, microspores) and then cultures these cells within a culture medium (see Konzak *et al.*, column 4, lines 14-18) supplemented with plant ovaries or plant ovary supplemented media. The Konzak *et al.* method may include an optional transformation, but this is performed **after** the microspore is isolated by the preparative centrifugation step.

The Examiner further points to the Konzak *et al.* disclosure of "Microspores can be genetically transformed at any time during treatment of the microspores... (col.4, lines 33-36)." From this statement a skilled artisan would further discern that the centrifugation step is merely preparative in nature and that centrifugation and gene transfer efficiency are separate events and are completely independent from each other.

Forreiter *et al.* disclose centrifuging *Agrobacteria*, and then contacting *Arabidopsis* cells with *Agrobacteria*. **After 48 hours**, the *Arabidopsis* cells were washed, resuspended in culture

media, vortexed, and then collected by a short centrifugation step (1 minute at 600G). Forreiter *et al.* indicate that the transformation they followed occurred for 48 hours, then the cells were collected. Again, this centrifugation step is still preparative in nature and independent to the transformation event. Thus, the artisan would not be motivated to use a high *g* centrifugation method, because transformation efficiency would be assessed during the transformation event itself –when the cells were co-cultured for 48 hours with *Agrobacteria.* In fact, Forreiter *et al.* assesses transformation efficiency after the cells were co-infected (co-cultivation) (See Forreiter *et al.*, page 2172, Figure 1). The cells were plated onto agar plates and grown for three weeks. Forreiter *et al.* does not motivate the artisan to contemplate centrifugation for efficient transformation efficiency since they performed efficiency within cell culture alone.

As stated above, neither the Konzak *et* al., nor the Forreiter *et al.* reference alone or in combination teach or suggest the claim element of "centrifuging the plant, plant cells or plant tissues under a centrifugal acceleration of 1000G to 150,000G...wherein said centrifugation promotes efficiency of the transformation of the desired gene into said plant cell, tissue or plant."

As in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty.*, cited above, it remains necessary to identify some reason that would have led a researcher to modify Konzak *et al.* in a particular manner, in order to establish a *prima facie* case of obviousness. As a practical matter, Konzak *et al.* and Forreiter *et al.* teach away from the present invention since a skilled artisan, such as a biochemist or molecular biologist, would take the learnings from each reference and utilize the centrifugation methods within each as a preparative step, mainly to isolate a material from a mixture. An artisan is not motivated to use the approach in Konzak *et al.* since the methodology asserted by the Examiner is a purification scheme which involves a sugar density

gradient centrifugation to separate plant organelles. The artisan would not make the link of transformation efficiency and centrifugation, since Forreiter *et al.*, uses cell culture and time to assess transformation efficiency.

Therefore, Konzak *et al.* and Forreiter *et al.* teach away from the present invention and the *prima facie* case of obviousness has not been met.

Additionally, the Examiner asserts that even though the centrifugal acceleration is not taught in the combined references, the rate and time of centrifugation is a 'result effective parameter' that a person of ordinary skill in the art would routinely optimize. Thus, the Examiner asserts that absent some demonstration of unexpected results from the claimed parameters, this optimization of rate and time of centrifugation would have been obvious at the time of Applicants' invention. Applicants again respectfully traverse.

Applicants submit that unexpected results are achieved by increasing the centrifugal acceleration to between 1000G and 150,000G. That is, transformation efficiency is unexpectedly promoted by carrying out centrifugation of plants samples at centrifugal accelerations of 1000G to 150,000G. Applicants submit that a skilled artisan would not have expected these results based on the teachings and suggestions in the cited references. The above discussed references use centrifugation to merely separate plant debris and isolate particular plant organelles. Thus, Applicants contend that a skilled artisan would not have expected transformation efficiency to be significantly improved by using centrifugal acceleration in the range of 1000G to 150,000G.

The Examiner's assertion, "optimization of parameters" seems to mean "optimization of centrifugation speed as a parameter of gene transfer efficiency." However, in neither of Konzak *et al.* nor Forreiter *et al.*, a description nor suggestion of a relation between centrifugation and

gene transfer efficiency can be found. One cannot optimize a parameter in cases where no relation can be found between centrifugation and gene transfer efficiency. The scientific fact that "centrifugation speed is a parameter of gene transfer efficiency" is first discovered by the present inventors, and this discovery itself is the very basis of the present invention. Therefore the Examiner's assertion above is a mere hindsight based on the present invention.

The Examiner attempts to point out a relation between centrifugation acceleration and rotor size. However, this argument does not make sense since no relation can be found between centrifugation and gene transfer efficiency in either of the cited documents.

The Examiner further points out that the results of gene transfer efficiency disclosed in the present application are inconsistent, thus centrifugation over 1000G does not seem to significantly elevate gene transfer efficiency.

To this assertion, and the assertion cited above regarding optimization of rate and time of centrifugation would have been obvious at the time of Applicants' invention, Applicants respectfully traverse, and herein submit a 37 CFR § 1.132 declaration, which clearly shows that gene transfer efficiency is improved in a centrifugation speed dependent manner.

Therefore, claim 22-29 are not obvious over the combination of Konzak *et al.* and Forreiter *et al.* references. Accordingly, Applicants respectfully request the rejection be reconsidered and withdrawn.

In view of the above, Applicants believe the pending application is in condition for allowance.

CONCLUSION

In view of the above remarks, it is believed that claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Paul D. Pyla, Reg. No. 59,228, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: NOV 1 3 2007

Respectfully submitted,

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Enclosure: 37 C.F.R. § 1.132 Affidavit